National Institute of Allergy and Infectious Diseases
National Institutes of Health

Division of AIDS **revised April 11, 2005**

Questions and Answers

Pre-Application Meeting for the Leadership for HIV/AIDS Clinical Trials Networks

Funding

1. DAIDS has indicated that there will be $300 million available for the HIV/AIDS Clinical Trials Networks. What does this cover?

The Division of AIDS (DAIDS) hopes to allocate a total of $300 million for the first year costs of the Leadership for HIV/AIDS Clinical Trials Networks, including the Protocol Implementation Funds and the Clinical Trials Units (CTUs). The actual amount of funding available for the Leadership and Units for HIV/AIDS Clinical Trials Networks will be contingent on FY 2006 appropriations. The final distribution of funds for the Network Leadership awards will be determined by DAIDS based on the results of the peer review, and the number, type and size of successful applications.

2. Are there separate funds available for the transitional costs associated with the phase-out of studies and the continuation of ongoing studies?

No. Funds to cover phase-out or continuation of existing studies in the first year of the awards will be allocated from the $300 million total available for the HIV/AIDS Clinical Trials Networks (Network Leaderships and Clinical Trials Units). Any money used to complete ongoing studies will reduce the amount of money available for new studies. Therefore, it is essential for applicants to set priorities for the completion of ongoing studies based on how well those studies fit the proposed scientific agenda and research plan.

3. Please clarify how funds will be allocated to the Clinical Trials Units.

The Clinical Trials Units will be funded at a base level. Budgets will be constructed to support CTU administration and the 'Core Costs' for each Clinical Research Site. The 'Core Costs' will identify the financial resources required to maintain Clinical Research Site(s) and meet the following Clinical Research Site capacity requirement: each Clinical Research Site must maintain an average monthly census of 20 study participants over a

12-month period for each proposed Network affiliation. Each Clinical Research Site within a CTU must recruit, screen, enroll and follow sufficient participants so that the average number of participants per month 'on study' is no less than 20 over a 12-month period. The minimum of 20 participants applies to each Network with which the Clinical Research Site is affiliated. (For example, if a Clinical Research Site is proposing affiliation with two Networks, the 'Core Costs' would include the costs to maintain an average of 20 participants per month over a 12-month period in a study (or studies) for Network A and 20 participants over a 12-month period in a study (or studies) for Network B.) Additional funds above this base level will be allocated to CTUs through the Protocol Implementation Fund. Those funds will be managed by the Network Leadership and will be dispersed based on the current research priority and the performance of individual units. DAIDS/NIAID will oversee the distribution of funds.

4. What is the DAIDS Reserve Fund?

DAIDS intends to reserve a portion of the total funds from the entire allocation for the HIV/AIDS Clinical Trials Networks to establish the DAIDS Reserve Fund. Reserve funds will be made available to the Networks to support new scientific opportunities and changing research priorities. The establishment of the Reserve Fund will be contingent on the availability of funds to DAIDS. DAIDS anticipates establishing the DAIDS Reserve Fund during the second budget period of the Network Leadership awards.

5. Will additional funding be available to coordinate the activities of the Community Partners?

Yes. DAIDS will provide logistical and operational support to the Community Partners. In addition, the Networks and Clinical Trials Units are expected to: fund Community Advisory Boards at a level that will enable their appropriate representation in the Community Partners; support the Network's contribution to the development of Community Partners initiatives; and implement Community Partner recommendations.

The Community Partners will be established to promote effective representation of, and timely communication among, the many communities, domestically and internationally, working with the Clinical Trials Networks. Membership for the Community Partners will be drawn from Network and Clinical Trials Units Community Advisory Boards as well as other groups.

6. Will additional funding/support be available to support and coordinate activities of the Managing Partners?

Yes. DAIDS will provide the Managing Partners with a separate budget to facilitate communication and coordination across the Networks. DAIDS anticipates that expenses for cross-Network harmonization and coordination activities sponsored by the Managing Partners will be shared appropriately among the involved entities, including Network Leadership components (Coordinating and Operations Center [CORE], Statistical and Data Management Center [SDMC] and/or Network Laboratory Structure [NLS]), and the

DAIDS contract resources supporting clinical research. Specific arrangements are likely to vary and depend upon the scope and complexity of an activity or project.

Research Plan

1. Should the application be structured along the high priority research areas delineated in the RFA?

Yes, the application should be structured and assembled as delineated in the RFA. In order to facilitate the review process, applications will be evaluated according to the scientific priority being addressed (e.g., Vaccine Research and Development, Translational Research/Drug Development, Optimization of Clinical Management including Co-Morbidities, Microbicides, Prevention of Mother to Child Transmission of HIV, and Prevention of HIV Infection).

2. If an applicant identifies more than one high priority research area in the research plan, must all elements of that research area be addressed?

No. A Network Leadership applicant is not required to address all of the elements within a research priority. However, the proposed research plan should clearly identify those research priorities and elements that will be addressed in full and those that will be addressed in part, and whether they will be addressed by the Network alone and/or in collaboration with other Networks, agencies/organizations, or other Institutes and Centers at the National Institutes of Health (NIH).

3. How should a group describe research that addresses more than one high priority research area? For example, if a group is planning to describe vaccine trials for prevention of breastfeeding mother-to-child HIV transmission, should the proposed activities be described in the PMTCT section or Vaccine section of the application? Since each of the six priority research sections of the RFA will be evaluated by separate review panels should research activities be described in multiple sections of the application?

DAIDS understands that there will be some degree of overlap across the six priority research areas. However, it is recommended that applicants determine which priority research area is best aligned with the primary goal of the proposed research.

In the above case, if the primary goal of the group is to identify a safe and effective vaccine, then plans should fall under the Vaccine section of the RFA. If the primary research goal is PMTCT, the plans should be outlined under the MTCT section of the RFA.

Applicants should not duplicate research outlines in multiple sections of the application. However, after activities have been fully described in the most appropriate section, applicants may choose to briefly reference these activities in subsequent sections.

In the interest of harmonization across Networks, applicants are encouraged to propose strategies to coordinate with other Network Leadership in cases where the primary goals of one Network are the secondary goals of the other, and vice versa.

Please note that while the priority research areas and Network Leadership components will be assessed by separate groups, the final stage of review will include a comprehensive review of the entire application.

4. Do all of the elements within a given research priority carry the same level of importance?

No. The different elements within a given research priority should not necessarily be considered of equal importance. Members of the peer review panel will apply standard NIH review criteria as well as the specific criteria identified in the RFA to assess the significance, approach and innovation of the proposed research plan. The slides from the pre-application meeting, posted at http://www.niaid.nih.gov/daids/rfa/network06/pdf/Preapp5a.pdf, indicate those elements within a given research area that are of highest priority to NIAID (shown in black), those that are likely to require partnering and/or additional resources to fully accomplish (shown in grey) and those that are priorities to NIAID's research partners at other NIH Institutes and Centers (shown in blue). Please note that the RFA is not color coded to make these distinctions.

Application Options, Application Assembly and Page Limits

1. Is there a review advantage for a Network Leadership to submit 3 separate applications for CORE, Network Laboratory Structure and Statistical and Data Management Center components? Is there a review advantage for a Network Leadership to submit one application that includes all three components?

No. Applicants are offered the option of proposing an HIV/AIDS Clinical Trials Network through one, two or three applications so that successful applicants will have the most efficient and effective organizational structure for the Network. Specific review panels will be established to review specific components and high priority research areas. All Network applicants must adhere to the same page limits, whether they have submitted one, two or three applications.

2. The application Web site contains the "Suggested Summary Sheet and Tables for a Leadership Application." Is the use of these forms required?

No. DAIDS has provided the summary sheet and tables as examples that contain the relevant information in a standard format. The use of these specific forms is recommended but cannot be mandated.

3. If the application for Network Leadership includes more than one component, is the Network Overview still limited to 20 pages?

Yes. The section titled 'Network Overview' is limited to 20 pages. An identical 20-page limit Network Overview should be included in each application submitted by a Network Leadership. Thus, if a Network submits three separate applications for the CORE, SDMC and NLS, each application should include an identical 20-page Network Overview. If two applications are submitted, they should each include an identical 20-page Network Overview. If all three Network components are included in the Network Leadership application there should be one section titled Network Overview and it has a 20-page limit.

4. Are transition plans and the required tables included in the 150-page limit?

For large Networks, which may have between 40 and 50 studies that will be phased out or continued, the transition plans/tables will be quite extensive and would limit the number of pages that can be devoted to the description of future research plans. Recognizing that large Networks may have a significant amount of ongoing work, DAIDS has decided that Table 4 and Table 5 (found at www.niaid.nih.gov/daids/rfa/network06) will not count against the page limit.

These tables were developed to assist applicants in providing necessary information in a convenient format and to reduce the number of pages needed to describe transition plans. DAIDS is modifying the RFA to exclude these tables from the page limit and a note will appear in the NIH Guide to this effect. The significance of and rationale for the continuation of specific studies should be included in the Network Research Plan. The description of these transition plans will be counted in the 150-page limit.

5. If a Network Leadership group is submitting an application with three separate U01s for the components, it seems that the same identical face page would be included with each submission. Is that correct?

No. The face page for each U01 application must reflect the appropriate U01 component, such as the title, institution, Principal Investigator, and budget. Each application should also contain a page similar to the DAIDS proposed Summary Sheet (available through the application Web site) that identifies the application Network affiliation. Additionally, a section titled Network Overview should be included in each Network application and should be identical in each.

6. The RFA states that the appendix is limited to 30 pages. Are the 30 pages to be divided among the component U01 applications or is it 30 pages per application?

Each Network Leadership component is allowed an appendix of 30 pages. For example, an application with one component is allowed an appendix of up to 30 pages, while an application consisting of two components is permitted two appendices, each limited to 30 pages.

7. Do all of the face and cover pages in the applications need to have original signatures?

The face page for each individual U01 application must include the required signature of the Principal Investigator and the Authorizing Business Official. Original signatures are not needed on cover pages for individual components contained within an application.

Budget

1. How should budgets be prepared? Should they be broken down by Network function and by research priority area?

The budgets for each Network component should be summarized in a composite PHS 398 Page 4 (initial budget period) and Page 5 (entire budget period). Separate functions (e.g., CORE administrative support, CORE coordination and logistic support) should be presented in separate budget pages as described in the application instructions. All budgets should be divided by budget category (e.g., salary, fringe benefits, consultant, equipment). Separate budgets should not be prepared for each priority research area. Instead, the percentage of the total budget of the CORE, NLS or SDMC that each scientific priority constitutes should be stated in the budget justification.

2. If a Network proposes research in multiple high priority research areas, is a proportionate breakdown required in the budget?

The budget itself should not be broken down by the different research areas. It should be broken down according to Network component, functions as identified above, and by budget periods (years). However, the budget justification should reflect the percentage breakdown by research area. For example, of the total SDMC budget, 50% is for one area of research, 20% for another and 30% percent for another.

3. Does the application need to include the rationale for how these percentages were derived?

No, that level of detail is not required; however, it is expected that the requested budget items should be justified and the percentage appropriately reflect the scope of the proposed work.

4. Are the budgets of the Network Leadership components (e.g., the Statistical and Data Management Center, Network Laboratory Structure, and CORE) to be fixed or variable?

The budget for each Network component should be developed based on the volume of clinical research activity equivalent to “Core Costs” for the Clinical Research Sites. The type and volume of activity should reflect the capacity requirement that each Clinical Research Site maintain an average of 20 participants ‘on study’ per month over a 12

month period. It is planned that additional resource requirements for each Network component to implement the proposed research plan in its entirety will be disbursed by the Network through the Protocol Implementation Fund administered by the CORE. Costs to complete ongoing studies, known as 'transition costs' for each Network component should be included only in the Transition Costs budget in the CORE application.

5. How should transition budgets be prepared?

The actual cost of completing and phasing out ongoing trials should be estimated by the Network assuming responsibility for the study. While the currently funded Networks do not capture cost information in the same way it is being requested in the RFA, applicants are asked to provide this information to the best of their ability in the format provided (See Table 4, which can be found at http://www.niaid.nih.gov/daids/rfa/network06/pdf/Table4.doc).

6. Does the application need to include the estimated cost of proposed studies?

Yes. The budget for each Network component should be based on volume of clinical research activity equivalent to the total Clinical Research Capacity Requirements ("Core Costs") for the proposed Clinical Research Sites. Additional resource requirements for each Network component will be disbursed by the Network through the Protocol Implementation fund. The Protocol Implementation Fund formula(s) developed by the applicant should be applied to the clinical research activities proposed in the application. "Table 5: Proposed Clinical Research Activities" (http://www.niaid.nih.gov/daids/rfa/network06/pdf/Table5.doc) provides a convenient format for identifying proposed clinical research activities and determining the costs for each Network component and the sites. Table 5 will not be included in the page limits.

The "Core Costs" for each Network component should be included in the Detailed Budget for the Initial Budget Plan and the Budget for Entire Proposed Period of Support for that component.

The difference between the Table 5 Total and the "Core Costs" for each component (CORE, SDMC, and NLS) and Clinical Research Sites for the first year only should be reported in the CORE budget. This figure should be included in the "Other Expenses Section" on the Transition Costs Detailed Budget Page for the Initial Budget Period and for the Budget for Entire Proposed Project Period. Details for subsequent budget periods (years 2-7) are requested for planning purposes and should not be included in the composite budget pages.

7. In resource-limited settings, does funding for routine testing and clinical monitoring fall within the protocol budget or the laboratory budget?

Budgeting for routine laboratory testing and clinical monitoring (i.e., the type of tests usually performed locally) should be included in the Clinical Research Site "Core Costs"

in the applications for the Clinical Trials Units RFA, not the Network Laboratory Structure budget. Additional resources to support laboratory testing for participants in excess of the Clinical Research Site capacity requirements (over an average of 20 participants/month) will be reflected in the Protocol Implementation Fund in the Network CORE budget.

8. Will 'science' at the Clinical Research Sites be supported through the CTU and Site budgets and/or the Network Leadership budget?

It is the responsibility of each Network Leadership to propose and budget for the scientific research plans and questions that it feels must be addressed to meet its research goals. This should include protocol implementation capabilities required of the Clinical Research Sites (beyond the Site's 'Core Costs') and/or any proposed site-specific studies. Each CTU will receive funding for 'Core Costs' needed to maintain its affiliated Clinical Research Site(s) and the minimum capacity required. Additional support for site research activities will be funded by the Network's Protocol Implementation Fund (for protocol-linked studies) or by the Network CORE budget (for cross-cutting research such as cross-protocol studies). This will ensure that all science conducted at the site level is appropriately related to the Network's scientific plans. Clinical Research Sites will be accountable to each Network Leadership with which they are affiliated for the research conducted on behalf of that Network. In turn, the Network Leadership will be accountable for their overall research activities, including those of participating Clinical Trials Units and Clinical Research Sites.

Clinical Trials Units

1. How can applicants for the Network Leadership identify CTUs and construct a CORE budget without specific knowledge of CTU plans, (e.g. the number of administrative CTUs and associated sites)? Most institutions have not yet decided how they will be organized.

The RFA to solicit Clinical Trials Units was recently released. Network applicants should be able to identify the number of required participants as well as the approximate number and size of required Clinical Research Sites needed to enroll participants from populations most impacted or threatened by HIV/AIDS and to implement the proposed Network research plan. DAIDS recognizes that final decisions regarding Network and CTU affiliation may not be made at the time the Leadership applications are due. Nevertheless, Network Leadership applicants should propose the CTUs (and/or Clinical Research Sites) to the best of their ability and complete Table 3: Potential Clinical Trials Units and Clinical Research Sites. Network Leadership applicants should plan to provide letters of commitment to applicants for Clinical Trials Units.

In addition, NIAID will make available a Web site for the voluntary sharing of information among applicants to the "Leadership for HIV/AIDS Clinical Trials Networks" and "Units for HIV/AIDS Clinical Trials Networks." Applicants may, at their

choosing, use this Web site to share information about applicant Network clinical research plans and Network capacity needs, as well as the interests and availability of Clinical Trials Units and Clinical Research Sites. NIAID will accept and post information, statements of interest, and contact information. Instructions for submitting information for posting is available at http://www.niaid.nih.gov/daids/rfa/network06. All postings will remain on the Web site until the final receipt date for applications."

2. It is difficult for the Network Leadership to identify which CTUs should be phased out. Doing so could create tension between the Leadership and a Unit that has the potential of still being funded but is not identified in the Network's application. It is also difficult to present a list of phase-out units without a better understanding of the Units for HIV/AIDS Clinical Trials Networks RFA.

It is the responsibility of the Network Leadership to identify the approximate number of Clinical Research Sites required for efficient and effective implementation of the clinical research plan as well as to identify Clinical Research Sites best suited for enrolling participants who are representative of those populations most severely impacted by HIV/AIDS. Network applicants must identify Clinical Trials Units and Clinical Research Sites with these and other characteristics that make them best suited to accomplish the proposed research plan.

3. Will currently-active sites that are not successful in competing in a future Network be allowed to complete the trials they are already conducting?

DAIDS will work closely with the Networks to develop and implement a plan for the continuation and/or phase-out of clinical trials and clinical trial sites. Decisions regarding the continuation of individual sites are likely to occur on a case-by-case basis and take into consideration the priority of the ongoing clinical research, the performance of the clinical trial site, and the rationale for the site's continued involvement.

4. Please clarify the requirement of having 20 patients per Clinical Research Site.

Each Clinical Research Site must maintain an average monthly census of 20 study participants over a 12-month period for each Network. Each Clinical Research Site within a CTU must recruit, screen, enroll and follow sufficient participants so that the average number of participants per month 'on study' is no less than 20 over a 12- month period. The minimum of 20 participants per Clinical Research Site applies to each Network with which the Clinical Research Site is affiliated.

Protocol Implementation Fund

1. Do applicants need to specify how they plan to develop the budget for the Protocol Implementation Fund or do they need to estimate the costs associated with the proposed scientific agenda?

Applicants should indicate what *types* of costs will be included in the Protocol Implementation Fund. In addition, they should include how budgets will be developed, finalized, and negotiated as well as who will make decisions about how the funds will be dispersed. DAIDS Table 5 is constructed so as to identify proposed clinical trials and, using formulas described for the Protocol Implementation Fund, identify the overall costs for each study at each Network component (CORE, SDMC, NLS, and the Clinical Trials Units). Applicants are reminded that the Protocol Implementation Fund covers the costs of trials above what is included in the core budget.

2. Does the Protocol Implementation Fund support the scientific contributions of Unit investigators in their role as protocol chair?

Yes, it can. The Protocol Implementation Fund is intended to support all costs above core costs associated with protocol development and implementation, and can include the costs associated with funds for the Protocol Chair and Protocol Team members. The Protocol Implementation Fund is not intended for salary support for the scientific leadership contribution of key personnel (e.g., CTU investigators). These costs should be included in Network Leadership budgets.

3. Is the Protocol Implementation Fund part of the CORE budget or will it be allocated to the CORE separately?

The Protocol Implementation Fund is a separate allocation. Each Network Leadership application must specify how the Protocol Implementation Fund will be distributed and the protocol-specific development/implementation costs that it will be used to support.

4. Will the Protocol Implementation Fund be used only to support new studies?

No. The Protocol Implementation Fund will be used to support all studies (newly-proposed as well as ongoing studies) that will continue to be conducted as part of the newly-established Network. DAIDS suggested Tables 4 and 5 have been constructed in order that both applicants and NIAID can distinguish costs associated with ongoing clinical research protocols (open to enrollment, closed to enrollment, or pending enrollment) and research newly proposed through this application.

Investigator and Clinical Trials Unit Staff Support for Network Activities

1. How should the scientific contributions of investigators and other Clinical Trials Unit staff be budgeted (e.g., investigators/staff who play an active role on the Executive, Scientific and/or Resource Committees)?

The scientific effort of investigators and other CTU staff who play an active role as Committee Chairs and Vice-Chairs or in other capacities in the Network Leadership should be addressed in the CORE budget of the Network Leadership application. Funds

for Protocol Chairs and team members can be addressed in the plans for use of the Protocol Implementation Fund.

Committee Structure

1. The RFA specifies the required committees of each Network Leadership, namely an Executive, Scientific, and Resource Committees and a Community Advisory Board. Do applicants need to establish each of these committees or can the functions be addressed within a different committee structure?

Each Network Leadership must include an Executive Committee, Scientific Committees as appropriate, a Network Community Advisory Board, and the Resource Committees identified in the RFA. However, if applicants consider it more efficient to combine the required Resource Committee functions they can do so. The title of the resulting integrated committee should reflect the combined functions (e.g., Data Management and QA/QC Committee). Reviewers will look to see that each committee function is adequately addressed in the application regardless of how the committee(s) is/are actually established or where it/they fit within the structure of the Network, e.g., independent committee(s) or subcommittee(s).

2. Should applicants list the names of investigators who will be participating in Executive, Scientific and/or Resource Committees?

It is important to name the individuals who will have key roles in the Network Leadership and who are members of internal Network committee. However, it is recommended that applicants do not list the names of potential members of external or advisory committees. Doing so would greatly limit the eligible pool of reviewers.

3. If key individuals are not named in the application, won't review activities be compromised if these individuals serve as reviewers without acknowledging their potential role in one of the Networks?

Staff in NIAID's Division of Extramural Affairs (DEA) will work diligently to ensure that the review groups are established without any conflict of interest. While it is important to name internal committee members and individuals with key leadership roles, it is strongly recommended that the application does not identify those who are to consult on an as needed basis or have not confirmed their willingness to fulfill important, but essentially external advisory roles.

Laboratory

1. Where should laboratory research questions, as opposed to other laboratory support activities, be described? What part of the Laboratory cost and infrastructure related to routine laboratories and safety monitoring should be included in the NLS and what

part should be considered a Clinical Trials Units cost, including for international Units?

The description of and budgeting for laboratory activities will be included in one of four places:

Network CORE (Network Leadership Application): Hypothesis-driven laboratory research related to the research agenda should be described in the Network CORE application. For example, retrospective ancillary studies to explore research questions that are not included in trial designs but that relate to the Network research plan may be proposed. Such studies should be described in the Network research plan in the CORE application as well as a review process and mechanism to approve specimens.

Network Laboratory Structure (Network Leadership Application):
Any research proposed in the Network Laboratory Structure application should be directly related to the Network research agenda. The NLS budget should include the costs of protocol-related central laboratory testing required by the Network for the first 20 patients "on study" for each Clinical Research Site. These tests could include endpoint immunogenicity assays, routine monitoring of HIV serostatus throughout and after vaccine trials, external quality assurance for domestic and international clinical safety testing, external quality assurance for PBMC processing, external quality assurance for immunologic and virologic endpoint monitoring laboratories, and central specimen storage, shipping and redistribution. Protocol-related central laboratory costs for additional participants should be budgeted for in the Protocol Implementation Fund. (See question #4 under "Budget" for more information.) .

Other activities described in the NLS application may include the need to transition a research and development assay to an assay that is standardized and validated for use as an endpoint, and prospective ancillary studies that involve the use of a new technology or assay development.

CTU "Core Funding" (Clinical Trials Units Application): Applicants responding to the RFA 'Units for HIV/AIDS Clinical Trials Networks' will be constructing budgets based on Clinical Research Site 'Core Costs,' i.e., the funds required to maintain a Clinical Research Site, including laboratory resources as necessary, and the costs to recruit, screen, enroll and follow sufficient participants so that the average number of participants per month 'on study' is no less than 20 over a 12-month period. The minimum of 20 participants per Clinical Research Site applies to each Network with which the Clinical Research Site is affiliated.

Sample protocol schemas will be provided on the RFA Web site to assist in budget development. CTU budgets should include the performance of routine safety tests to ensure a participant's safety while on a clinical trial (e.g., pregnancy tests, blood chemistries, functional tests such as urinalysis, STD testing, CD4 counts, viral loads), as well as costs incurred locally for specimen processing, specimen storage, shipping and redistribution.

Protocol Implementation Fund (Network Leadership Application): Funds to support participation over and above the Core Clinical Research Site Capacity requirements (i.e., exceeding an average of 20 participants/month) should be included in the Protocol Implementation Fund.

Budgeting CTU and Network-associated Laboratory Activities	
ACTIVITY	**WHERE TO BUDGET**
Protocol-related local laboratory testing (first 20 subjects)	CTU budget
Protocol-related local laboratory testing (>20 subjects)	Network CORE (Protocol Implementation Fund)
Protocol-related central laboratory testing (first 20 subjects)	NLS budget
Protocol-related central laboratory testing (>20 subjects)	Network CORE (Protocol Implementation Fund)
Network-specific QA activities	NLS
Hypothesis-driven laboratory testing	Network CORE

2. Can funds for the Network Laboratory Structure be used to develop new assays?

Funds for the Network Laboratory Structure may not be used to implement novel assays within the context of the research agenda. NLS funds are not, in general, for use in new assay development, except if key research questions of high priority require the development, standardization or development of a novel assay to support testing of a novel hypothesis or product. As previously noted, hypothesis-driven scientific research, whether or not laboratory based, should be included in the Network CORE Research Plan.

3. There doesn't appear to be room for multi-disciplinary laboratories that cover pharmacology, virology, and immunology. Please clarify.

The RFA does not specify, require or preclude any particular configuration of laboratories (multidisciplinary or otherwise). The proposed Network Laboratory Structure should address the proposed approach to meet the needs required to carry out the Network's research plan.

4. If there are multiple laboratories proposed as part of the Network Laboratory Structure, must each laboratory Principal Investigator commit to 50% effort or is the specification applicable only to the overall Principal Investigator of the Laboratory Group? Can the 50% effort be shared by multiple Laboratory investigators?

Each Network Leadership application shall propose a Network Laboratory Structure for which there is one Principal Investigator at 50% effort. Other laboratory directors/investigators can contribute to the NLS at percent efforts determined by the Principal Investigator of the Network Laboratory Structure.

5. Can several Network Leadership applicants submit a single, joint application for laboratories that will service all the Networks?

No. Each Network Leadership applicant must submit its own application for a Network Laboratory Structure component. However, the RFA makes clear that Networks, institutions and investigators with laboratory (as well as other) expertise are encouraged to participate in and/or collaborate with other DAIDS and NIH-sponsored Clinical Trials Networks.

6. Should laboratory Quality Assurance/Quality Control functions, which are expensive, be a cross-Network function or a function of the Laboratory component?

All Network-required laboratory work should be part of a Network-specific laboratory component and not a cross-Network function. However, an external Quality Assurance program that transcends common Network actitivities is conceivable as a cross-Network function. If and when such cross-Network functions are put in place, adjustments to the work and budget of each Network will be made.

7. Should the Network Leadership application identify specific laboratories for central testing or should it simply describe the process that will be used to select central laboratories?

Central laboratories, including organization, personnel and infrastructure, for protocol-specific work should be identified in an application as they are key components of the Network Laboratory Structure.

Statistical and Data Management

1. Can there be a core budget for the Statistical and Data Management Center or must all of the costs be allocated on a percentage basis to a given research area? What happens if one or more specific areas are cut, but the costs are not divisible?

As stated in the RFA, all Statistical and Data Management Center costs should be allocated on a percentage basis by research area. If one particular research area is removed from the Network's proposed research plan, the budget will be negotiated at the time of award.

2. Will the Managing Partners drive data coordination? Shouldn't another group be established for this purpose that includes those with expertise in the area of data management?

The Managing Partners will have overarching responsibility for all coordinated activities among the Networks, including data collection and management. It is expected that the Managing Partners will utilize the skills of Network leaders and staff as well as external expertise, as necessary, to guide data coordination.

3. Will additional funding/support be available to support the development of common datasets, which will include numerous conference calls, interaction and input from experts?

Yes. Additional funds, above "core costs" will be provided for the coordination of common datasets. The Managing Partners, although not supported in this solicitation, will have its own budget. A portion of the costs for the development of common datasets should come from the Managing Partners, the Network CORE budget, and the Statistical and Data Management Center. In addition, DAIDS may provide additional resources through a variety of clinical research management support contracts that can assist in advancing this (and/or other) cross-Network coordinating activities.

4. It appears that the statistical component of a newly-formed Network will only include work associated with proposed studies (since other costs will be accounted for in the transitions plans). Is this correct?

This may be correct; however, it is assumed that 'new' Network structures that evolve from existing Network structures will assume responsibility for completion of ongoing work at its CORE, NLS, SDMC, and clinical trial sites.

5. For new SDMCs, the budget will be lower initially as compared to out years, since the earlier work is developmental in nature. As studies get underway, the level of effort/cost involved for the SDMC as a result of analyses will increase. Is this correct?

This is correct if one assumes that the SDMC for a new Network has no ongoing work at the time of award.

Support Contract Costs

1. Should Network Leadership CORE budgets include activities that ultimately will be handled by the DAIDS Clinical Research Management Support Contract (e.g., training)?

Yes. Since a Clinical Research Management Support (CRMS) Contract is not yet in place, the costs associated with all activities required for Network operations should be included within the appropriate Leadership component budget.

2. Will DAIDS continue to support the Regulatory Compliance Center that is currently funded under a separate contract?

DAIDS will continue to provide a variety of types of support and services (e.g., RCC) to the Clinical Trials Networks and other DAIDS-sponsored clinical trials. In the regulatory area, these would include:

- Preparation of IND submissions
- Receipt and processing reports of Serious Adverse Events
- Review of protocols and informed consents for compliance with regulations
- IND management support to DAIDS
- Safety monitoring of all DAIDS IND trials in conjunction with DAIDS Medical Officers during the protocol generation process
- Distribution of original and all subsequent IND submissions to the FDA, the participating pharmaceutical company, and parties within DAIDS
- Processing of site/protocol registration and assurance that each site has appropriate protocol registration documents prior to protocol initiation.

The Operations Centers component of each Network Leadership should still identify how it will manage any regulatory documents it receives (e.g., assurances).

Cross-Network Coordination

1. The RFA lists the submission of a Cross-Network Coordination Plan as a post-award activity, yet review criteria include cross-Network collaboration. Please explain.

The detailed Cross-Network Coordination Plan is required within 120 days of award to the individual Networks. However, applicants are expected to identify general ways in which they propose to work with other Networks to harmonize various activities and pursue research goals. For example, an application should note if laboratory resources within one Network can be used by other Networks to support cross-Network studies. Applicants can also describe how they will contribute to, and collaborate with, other Networks in support of research in scientific priority areas that other Networks are likely to pursue. Reviewers will be apprised of what they can reasonably expect from applicant groups regarding collaboration/coordination, and will be briefed in advance on these matters so they will understand what is appropriate for the review.

2. Are the Cross-Network Coordination Plans, including a number of very specific elements (e.g., specimen management) noted in the RFA, to be included in the 150-page limit?

The Networks need to propose and budget for all essential activities, including cross-Network activities. Later, if and when cross-Network activities are put in place, then that activity and associated dollars can be removed from the specific Networks.

3. To what extent should applicants be contacting and working with other NIH Institutes in developing their application?

The Division of AIDS has been working to facilitate interactions with other NIH partner Institutes. Applicants are encouraged to contact DAIDS and/or the other partner Institutes directly about their mission and scientific priorities. While neither DAIDS nor the other Institutes can provide advice or consult about the structure of an application, additional information about the scientific goals and priorities of the partner Institutes may help applicants in developing their research plans.

Review

1. If an applicant responds to more than one scientific priority and each of the scientific priority areas are reviewed separately, , how will the totality of the research plan be considered?

Special Emphasis Panels (SEPs) will be established for the six priority research areas, as well as for the Statistical and Data Management Center and Network Laboratory Structure. Each panel will receive the entire application package and will be asked to focus on only the relevant portion of it. Summaries from each SEP will then go to a Master Special Emphasis Panel, which will include members of the other SEPs, and additional members with expertise in the management and coordination of large, multi-institutional programs. This Master SEP will then award the overall scores for the CORE components and the combined applications. Scores will be given for each scientific area proposed, each component (CORE, NLS, and SDMC) and each application as a whole.

2. Will the scores assigned by the Special Emphasis Panels reflect the area of scientific priority being addressed? Are the scientific priorities weighted differently for review purposes?

No. While applicants must address one or more the six high priority research areas that are identified in the RFA, the scientific priorities are not weighted for scoring purposes.

DAIDS will work to achieve a balanced portfolio and assure its highest scientific priorities are adequately addressed in deciding the final awardees.

3. Are individuals involved in an advisory capacity with existing networks in conflict for reviewing new applications?

Not necessarily. Conflicts will be determined by a variety of criteria, including the nature of the advisory work and the specifics of the new applications.